IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

MAR 13 7006

Thomas M. DiMauro, Mohamed Attawia, Hassan Serhan, Martin A. Reynolds, Melissa Grace, Sudhakar Kadiyala, David Urbahns, Scott Bruder, Gregory Collins, Laura J. Brown, Jeffrey Geesin, Pamela L. Plouhar, Catherine W. Smith,

and John Siekierka

Sication No.:

10/630,227

Group Art Unit:

1647

Filed:

July 30, 2003

Examiner:

S.H. Shafer

Confirmation No.:

8291

Title:

Sir:

TRANS-CAPSULAR ADMINISTRATION OF HIGH SPECIFICITY CYTOKINE INHIBITORS INTO ORTHOPEDIC JOINTS

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, or is being facsimile transmitted to the United States Patent and Trademark Office on:

March 9, 2006

Date

da M. Rumes

Typed or printed name of person signing certificate

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

| This | Information Disclosure Statement is submitted: |
|------|------------------------------------------------|
| [] | under 37 CFR 1.129(a), or |

(First/Second submission after Final Rejection)

[] under 37 CFR 1.97(b), or

(Within any one of the following time periods: three months of filing national application (other than a CPA) or date of entry of the national stage in an international application; or before the mailing date of a first office action on the merits in a non-provisional application, including a CPA, or a Request for Continued Examination).

| LX. | under | 37 CFR | 1.97(c) | together | with | either |
|------|-------|---------|---------|------------|---------|---------|
| L 41 | unaci | J/ CIIC | 1.77(0) | to gottier | ** 1011 | OILLIOI |

[] a Statement under 37 CFR 1.97(e), as checked below, or

[X] a \$180.00 fee under 37 CFR 1.17(p), or

(After the 37 CFR 1.97(b) time period, but before final action or notice of allowance, whichever occurs first)

under 37 CFR 1.97(d) together with:

a Statement under 37 CFR 1.97(e), as checked below, and

a \$180.00 fee under 37 CFR 1.17(p), or

(Filed after final action or notice of allowance, whichever occurs first, but on or before payment of the issue fee)

[] under 37 CFR 1.97(i):

Applicant requests that the IDS and cited reference(s) be placed in the application file.

(Filed after payment of issue fee)

| <u>S</u> 1 | taten | nent Und | der 37 (| CFR 1.97(e) | | | | |
|------------|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|
| [|] | Each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement; or | | | | | | |
|] |] | No item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of this Information Disclosure Statement. | | | | | | |
| <u>S</u> 1 | taten | nent Und | der 37 (| CFR 1.704(d) (Patent Term Adjustment) Applies to original applications (other than design) filed on or after May 29, 2000 | | | | |
| [|] | commi | unication ot receiv | information contained in the Information Disclosure Statement was cited in a son from a foreign patent office in a counterpart application and this communication yed by any individual designated in § 1.56(c) more than thirty days prior to the information Disclosure Statement. | | | | |
| [] | X] | Enclos | sed here | ewith is form PTO-1449: | | | | |
| | | [X] | Copie | s of the cited references (B15-B20 and C39-C115) are enclosed. | | | | |
| | | • | [X] | Copies of issued U.S. patents and published U.S. applications are not required and are not being provided. | | | | |
| ; - | | []. | Applie | s of the cited references are enclosed except those entered in prior application, U.S. cation No. [], to which priority under 35 U.S.C. 120 is claimed. [The earlier ation contains copies of the cited references.] | | | | |
| • | | [] | The list | sted references were cited in the enclosed International Search Report in a expart foreign application. | | | | |
| | | [] | The "o | concise explanation" requirement (non-English references) for reference(s) [37 CFR 1.98(a)(3) is satisfied by: | | | | |
| | | | [] | the explanation provided on the attached sheet. | | | | |
| | | | [] | the explanation provided in the Specification. | | | | |
| | | | [] | submission of the enclosed International Search Report. | | | | |
| | | | [] | submission of the enclosed English-language version of a foreign Search Report and/or foreign Office Action. | | | | |
| | | | [] | the enclosed English language abstract. | | | | |

}

| [] | | cant requests that the following rabel or apply the stamp"Non-Published IDS Rej | | | | |
|------------------------|---------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|--|--|
| Examiner's Initials | | | | | | |
| | | U.S. Patent Application No. [|], by [inventor(s)], filed [|], Docket No.: [] | | |
| | | U.S. Patent Application No. [|], by [inventor(s)], filed [|], Docket No.: [] | | |
| | | U.S. Patent Application No. [|], by [inventor(s)], filed [|], Docket No.: [] | | |
| | | Examiner | Date | - | | |
| | [] | A copy of each above-cited apparts any application filed on or after Image File Wrapper (IFW) systems. | r June 30, 2003, which has b | een scanned into the PTO's | | |
| | [] | A copy of each above-cited appropriate appropriate appropriate appropriate and U.S.C. 120 is claimed. | plication, including the curre on, U.S. Application No. [| nt claims, is enclosed, except], to which priority under | | |
| | | r is requested to return a copy of re considered with the next offic | | plications indicating which | | |
| It is re | quested | I that the information disclosed h | nerein be made of record in the | his application. | | |
| Metho | d of pa | yment: | | | | |
| [X] | | ck for the fee noted above is enc apanying Reply. A copy of this S | | cluded in the check with the | | |
| [] | Please | e charge Deposit Account 08-038 sed. | 30 in the amount of \$[| . A copy of this Statement is | | |
| [X] | Please charge any deficiency in fees and credit any overpayment to Deposit Account 08-0380. | | | | | |
| | | I | Respectfully submitted, | | | |
| | | I | HAMILTON, BROOK, SMI | TH & REYNOLDS, P.C. | | |
| | | I | By Mish M. Doe | . Du | | |
| | | | Registration No.: 58,073 Telephone: (978) 341-0036 | | | |
| | | | Facsimile: (978) 341-0136 | | | |

Concord, MA 01742-9133
Dated: March 9, 2006

PTO-1449 REPRODUCED

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Use several sheets if necessary)

IN AN APPLICATION

FIRST NAMED INVENTOR Thomas M. DiMauro

ATTORNEY DOCKET NO.

3518.1015-000

APPLICATION NO. 10/630,227

FILING DATE July 30, 2003

March 9, 2006 **EXAMINER** S.H. Shafer CONFIRMATION NO. 8291

GROUP 1647

| Oran I | ADEAL LON | U.S | . PATENT DOCUMENTS | |
|-------------------------------|-------------|------------------------------------------------|------------------------------------------------|----------------------------------------------------|
| EXAM- INER INI- TIAL | REF. NO. | DOCUMENT NUMBER Number-Kind Code (if known) | ISSUE DATE / PUBLICATION DATE MM-DD-YYYY | NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT |
| | A22 | 5,510,370 | 04-23-1996 | Hock |
| | A23 | 5,833,984 | 11-10-1998 | Eibl, et al. |
| | A24 | 5,942,499 | 08-24-1999 | Radomsky |
| | A25 | 6,340,369 B1 | 01-22-2002 | Ferree |
| | A26 | 6,352,557 B1 | 03-05-2002 | Ferree |
| | A2# | 6,554,830 | 04-29-2003 | Chappius |
| | A28 | 6,590,081 B1 | 07-08-2003 | Zhang |
| | A29 | 6,623,472 B1 | 09-23-2003 | Reinecke, et al. |
| | A30 | 6,713,246 B1 | 03-30-2004 | Reinecke, et al. |
| | A31 | 2001/0006948 A1 | 07-05-2001 | Kang, et al. |
| | A32 | 2001/0026801 A1 | 10-04-2001 | Tobinick |
| | A33 | 2002/0010471 A1 | 01-24-2002 | Wironen, et al. |
| | A34 | 2002/0032155 A1 | 03-14-2002 | Ferree |
| | A35 | 2002/0107200 A1 | 08-08-2002 | Chang, et al. |
| | A36 | 2002/0198599 A1 | 12-26-2002 | Haldimann |
| | A37 | 2003/0007972 A1 | 01-09-2003 | Tobinick |
| | A38 | 2003/0069639 A1 | 04-10-2003 | Sander, et al. |
| | A39 | 2003/0207827 A1 | 11-06-2003 | Boyle, et al. |
| | A40 | 2004/0193274 A1 | 09-30-2004 | Trieu |
| | A41 | 2004/0229786 A1 | 11-18-2004 | Attawia, et al. |
| | A42 | 2005/0038001 A1 | 02-17-2005 | Attawia, et al. |
| | A43 | 2003/0134792 | 07-17-2003 | Pike, et al. |
| | A44 | 2002/0169162 | 11-14-2002 | Smith, et al. |
| | | | | |
| | | | | · |

| | | <u></u> |
|----------|---|-----------------|
| EXAMINER | | DATE CONSIDERED |
| | i | |
| 11 | i | |
| | [| |

PTO-1449 REPRODUCED

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION

March 9, 2006

(Use several sheets if necessary)

| ATTOR | NEY | DOCKET | NO. |
|-------|-----|--------|-----|
| 3518 | 101 | 5_000 | |

APPLICATION NO. 10/630,227

FIRST NAMED INVENTOR Thomas M. DiMauro

FILING DATE
July 30, 2003

EXAMINER S.H. Shafer

CONFIRMATION NO. 8291

group 1647

| | - | | OREIGN PATENT D | OCUMENTS | | | |
|---|-----|----------------------------------------------------------------|--------------------|---------------------------------------------------------------------------------|---------------|-----------------------|--|
| | | DOCUMENT NUMBER Country Code-Number-Kind Code (if known) | DATE MM-DD-YYYY | NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT | TRANSI YES | TRANSLATION YES NO | |
| | B15 | EP 0 950417 A2 | 10-20-1999 | Pfizer Products, Inc. | | | |
| | B16 | EP 1 464307 A1 | 10-06-2004 | DePuy Spine, Inc. | | | |
| • | B17 | WO 02/100387 A1 | 12-19-2002 | A+ Science Invest AB | | | |
| | B18 | WO 93/16099 A2 | 08-19-1993 | Biopharm Gesellschaft Zur Biotechnologischen Entwicklung Von Pharmaka MBH | | | |
| | B19 | WO 99/45923 A1 | 09-16-1999 | Merck & Co., Inc. | | | |
| | B20 | EP 1 153607 A2 | 11-14-2001 | Dunn | | | |
| | | | | · | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | · | | | | | |
| | | | | · | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | ļ | |
| | | | <u> </u> | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

| EXAMINER | DATE CONSIDERED |
|----------|-----------------|
| | , |

| PTO-1449 REPRODUCED | ATTORNEY DOCKET NO. APPLICATION NO. 10/630,227 | | | | |
|-----------------------------------------------------------------|------------------------------------------------|---------------|-----------------------------|---------------|--|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION | The | | filing date July 30, 200 | | |
| March 9, 2006 (Use several sheets if necessary) | EXAMINER S.H. Shafer | CONFI 8291 | RMATION NO. | GROUP 1647 | |

| | | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |
|---|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| - | C39 | Abstracts of the North American Spine Society 17 Annual Meeting, Montreal, Canada, October 29 through November 2, 2002, <i>The Spine Journal 2</i> (5 Suppl):49S-50S (2002). |
| | C40 | Ahn, N. U., et al., "Effect of Nutrient Concentration and OP-1 on the Metabolism of Intervertebral Disc: In Vitro Organ Culture Study," 28, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C41 | Alini, M. et al., "A Biological Approach in Treating Disc Degeneration: Not for Today, but Maybe for Tomorrow," European Spine Journal, 11(Suppl 2):S215-S220 (2002). |
| | C42 | Allali, F. et al., "Increase in Bone Mineral Density of Patients with Spondyloarthropathy Treated with Anti-Tumour Necrosis Factor α," Ann. Rheum. Dis., 62:347-349 (2003). |
| , | C43 | Andonopoulos, A.P., et al., "Intra-articular Anti-Tumor Necrosis Factor α Antibody in Recalcitrant Arthritis of Behçet's Disease," Clinical and Experimental Rheumatology 21(4 Suppl. 30):S57-58 (Jul-Aug 2003). |
| | C44 | Arai, I., et al., "Pretreatment with Loxoprofen Sodium, 6-OHDA or Anti TNF-Alpha Antibody Reduce Fos-Like Immunoreactivity in Rat Experimental Lumber Disc Herniation," 111, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C45 | Ariga, K. et al., "Mechanical Stress-Induced Apoptosis of Endplate Chondrocytes in Organ-Cultured Mouse Intervertebral Discs," Spine, 28(14):1528-1533 (2003). |
| | C46 | Biskobing, D.M., "Novel Therapies for Osteoporosis," Expert Opinion Invest. Drugs, 12(4):611-621 (2003). |
| - | C47 | Bokarewa, M., et al., "Local Infusion of Infliximab for the Treatment of Acute Joint Inflammation," Ann. Rheum Dis 62: 783-784 (2003). |
| | C48 | Burke, J. G., et al., "Human Nucleus Pulposus Secretes Transforming Growth Factor Beta-1 and Basic Fibroblast Growth Factor," 189, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C49 | Cardone, et al., "Diagnostic and Therapeutic Injection of the Hip and Knee," Family Medicine, 67:2147-2152 (2003). |
| | C50 | Connolly, J., et al., "Development of an Osteogenic Bone-Marrow Preparation," The Journal of Bone and Joint Surgery, Inc., 71-A (5): 684-691 (1989). |
| | .C51 | Conti, F., et al., "Successful Treatment with Intraarticular Infliximab for Resistant Knee Monarthritis in a Patient with Spondylarthropathy," Arthritis & Rheumatism 52(4): 1224-1226 (April 2005). |

| | |
|----------|-----------------|
| EXAMINER | DATE CONSIDERED |
| | |
| , | |

| PTO-1449 REPRODUCED | | | APPLICATION NO. 10/630,227 | |
|-----------------------------------------------------------------|----------------------------------------|---------------|-------------------------------|---------------|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION | FIRST NAMED INVENTOR Thomas M. DiMauro | | FILING DATE July 30, 2003 | |
| March 9, 2006 (Use several sheets if necessary) | EXAMINER S.H. Shafer | CONFI 8291 | RMATION NO. | GROUP 1647 |

| | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |
|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| C52 | Cornefjord, M., et al., "Cerebrospinal Fluid Biomarkers in Experimental Spinal Nerve Root Injury," 38, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C53 | Crandall, C., "Combination Treatment of Osteoporosis: A Clinical Review," J. of Women's Health & Gender-Based Medicine, 11(3):211-224 (2002). |
| C54 | DeSantis, A. and Buchman, A., "Current and Emerging Therapies in Osteoporosis," Expert Opin. Pharmacother., 3(7):835-843 (2002). |
| C55 | Diwan, A. et al., "Current Concepts in Intervertebral Disk Restoration," Tissue Engineering in Orthopedic Surgery, 31(3):453-464 (2000). |
| C56 | Edwards, S. L., et al., "Radiographic Assessment of Posterolateral Spine Fusion With and Without Platelet Rich Plasma," 117, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| . C57 | Ezra, A., and Golomb, G., "Administration Routes and Delivery Systems of Bisphosphonates for the Treatment of Bone Resorption," Adv. Drug Del. Rev., 42:175-195 (2000). |
| C58 | Frain, J., et al., "Use of cDNA Microarrays to Investigate Cytokine Expression in Intervertebral Disc Degeneration," 126, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C59 | Ganey, T. M. and Meisel, H. J., "A Potential Role for Cell-Based Therapeutics in the Treatment of Intervertebral Disc Herniation," Eur. Spine J., 11 (Suppl. 2): S206-S214 (2002). |
| C60 | Goodman, S. et al., "Effects of Local Infusion of TGFβ on Bone Ingrowth in Rabbit Chambers," J. Biomed. Mat. Res. (Appl Biomater), 53:475-479 (2000). |
| C61 | Goupille, P. et al., "Matrix Metalloproteinases: The Clue to Intervertebral Disc Degeneration?," Spine, 23(14): 1612-1626 (1998). |
| -C62 | Kawakami, et al., "Role of IL-8, MCP-1 and PH in Neuropathic Pain Enhanced by Degenerative Nucleus Pulposus," 127, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C63 | Hunter, C. J., et al., "Functional Behavior of Notochordal Cell Clusters in the Canine Nucleus Pulposus: Cell Communication and Survival," 70, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |

| EXAMINER | DATE CONSIDERED | , |
|----------|-----------------|---|
| | | |

| PTO-1449 REPRODUCED | ATTORNEY DOCKET NO. 3518.1015-000 | | APPLICATION NO. 10/630,227 | |
|-----------------------------------------------------------------|----------------------------------------|---------------|----------------------------|---------------|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION | FIRST NAMED INVENTOR Thomas M. DiMauro | | FILING DATE July 30, 2003 | |
| March 9, 2006 (Use several sheets if necessary) | EXAMINER S.H. Shafer | CONFI 8291 | RMATION NO. | GROUP 1647 |

| | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |
|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| C64 | Hydrogels, Encyclopedia of Polymer Science and Technology, (Wiley and Sons, 2003). |
| C65 | Imai, Y., et al., "Effect of Recombinant Human Osteogenic Protein-1 on Extracellular Matrix Metabolism by Human Annulus Fibrosus and Nucleus Pulposus Cells," 205, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C66 | Imai, Y., et al., "The Quantification of Cytokine-Induced Matrix Catabolism in Tissue Engeneered Intervertebral Discs," 67, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C67 | Inui, Y., et al., "Fas-Ligand Expression on Nucleus Pulposus Cells Begins in Developing Embryo," 42, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C68 | Karppinen, J., et al., "Tumor Necrosis Factor-α Monoclonal Antibody, Infliximab, Used to Manage Severe Sciatica," Spine, 28(8):750-754 (2003). |
| C69 | Kato, H., et al., "The Effect of IL-1 on the Rabbit Intervertebral Disc In Vivo," 199, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C70 | Kimble, R.B., et al., "Estrogen Deficiency Increases the Ability of Stromal Cells to Support Murine Osteoclastogenesis Via an InterLeukin-1 and Tumor Necrosis Factor-Mediated Stimulation of Macrophage Colony-Stimulating Factor Production," J. Biol. Chem. 271(46):28890-28897 (1996). |
| C71 | Kimble, R.B., et al., "The Functional Block of TNF but Not of IL-6 Prevents Bone Loss in Ovariectomized Mice," J. Bone Min. Res., 12(6):935-941 (1997). |
| C72 | Koch, H., et al., "Spontaneous Secretion of Interleukin 1 Receptor Antagonist (IL-1Ra) by Cells Isolated from Herniated Lumbar Discal Tissue After Discectomy," Cytokine, 10(9): 703-705 (1998). |
| C73 | Korhonen, T., et al., "Efficacy of Infliximab for Disc Herniation-Induced Sciatica One-Year Follow-Up," 14, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C74 . | Kozbor, D. and Roder, J.C., "The Production of Monoclonal Antibodies from Human Lymphocytes," <i>Immunol. Today, 4</i> (3):72-79 (1983). |
| C75 | Kwon, U-H., et al., "Dexamethsone Stimulates Cellular Proliferation While Downregulates Matrix Synthesis in Intervertebral Disc Cells," 29, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |

| EXAMINER | DATE CONSIDERED | |
|----------|-----------------|---|
| | | · |

| PTO-1449 REPRODUCED | ATTORNEY DOCKET NO. 3518.1015-000 | | .APPLICATION NO. 10/630,227 | | |
|-----------------------------------------------------------------|-----------------------------------|--------------|-----------------------------|----------------------------|--|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION | | | FILING DATE July 30, 200 | iling date uly 30, 2003 | |
| March 9, 2006 (Use several sheets if necessary) | EXAMINER S.H. Shafer | CONF 8291 | IRMATION NO. | GROUP 1647 | |

| | r | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |
|---|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| • | C76 | Lane, N.E., et al., "Basic Fibroblast Growth Factor Forms New Trabeculae that Physically Connect with Pre-Existing Trabeculae, and This New Bone is Maintained with an Anti-Resorptive Agent and Enhanced with an Anabolic Agent in an Osteopenic Rat Model," Osteoporos. Int., 14:374-382 (2003). |
| | C77 | La Van, et al., "Small-scale Systems for In Vivo Drug Delivery," Nature Biotechnology 21: 1184-1191 (2003). |
| | C78 | Lehman, et al., "Thalidomide Therapy for Recalcitrant Systemic Onset Juvenile Rheumatoid Arthritis," J. Pediatrics, 140: 125-7 (2002). |
| | C79 | Le Maitre, C. L., et al., "Expression of the IL-1 Family in Human Intervertebral Disc," 217, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C80 | Le Maitre, C. L., et al., "Response of Human Intervertebral Disc Cells to IL-1," 216, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C81 | Le Visage, C., et al., "Interaction of Human Mescenchymal Stem Cells with Disc Cells: Changes in Biosynthesis of Extracellular Matrix," 25, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C82 | Lee, C. S., et al., "A Single Period of Hyperphysiologic Stretch Induces IL-6, TGF-beta and Cell Proliferation in Anulus Fibrosus Cells," 215, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C83 | Li, J., et al., "The Effects of Bone Morphogenetic Protein 2 (BMP-2) and Cartilage-Derived Morphogentic Protein 2 (CDMP-2) on Aggrecan Gene Expression in Chondrocytes," 30, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C84 | Lotz, J. C., et al., "Cytokines in Normal, Degenerated, and Nucleoplasty-Treated Porcine Discs," 157, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| ' | C85 | Meijer, H., et al., "The Production of Anti-Inflammatory Cytokines in Whole Blood by Physico-Chemical Induction," Inflamm. Res., 52: 404-407 (2003). |
| | C86 | Miyamoto, H., et al., "The Effect of Mechanical Stress on the Production of Inflammatory Agents by Disc Cells," 110, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C87 | Molloy, et al., "The Roles of Growth Factors in Tendon and Ligament Healing," Sports. Med. 33: 381-394 (2003). |

| EXAMINER | | DATE CONSIDERED |
|----------|-----|-----------------|
| ' | | |
| | . i | |
| | | |

| PTO-1449 REPRODUCED | ATTORNEY DOCKET NO. 3518.1015-000 | | APPLICATION NO. 10/630,227 | |
|-----------------------------------------------------------------|----------------------------------------|----------------|-------------------------------|---------------|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION | FIRST NAMED INVENTOR Thomas M. DiMauro | | FILING DATE July 30, 2003 | |
| March 9, 2006 (Use several sheets if necessary) | EXAMINER S.H. Shafer | CONFII 8291 | RMATION NO. | GROUP 1647 |

| | | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | C88 | Müller, R. "Determination of Affinity and Specificity of Anti-Hapten Antibodies by Competitive Radioimmunoassay," <i>Meth. Enzymol.</i> , 92:589-601 (1983). |
| Nakamura, K., et al., "Local Application of Basic Fibroblast Growth Factor into the Bone Increases Bone Applied Site in Rabbits," Arch. Orthop. Trauma Surg., 115(6):344-346 (1996). | | Nakamura, K., et al., "Local Application of Basic Fibroblast Growth Factor into the Bone Increases Bone Mass at the Applied Site in Rabbits," Arch. Orthop. Trauma Surg., 115(6):344-346 (1996). |
| | ·C90 | Nakamura, K., et al., "Stimulation of Endosteal Bone Formation by Local Intraosseous Application of Basic Fibroblast Growth Factor in Rats," Rev. Rhum. [Engl. Ed.], 64(2):101-105 (1997). |
| | C91 | Nikas, S.N., et al., "Treatment of Resistant Rhematoid Arthritis by Intra-Articular Infliximab Injections: A Pilot Study," Ann Rheum Dis 63: 102-103 (2004). |
| | C92 | Ohtori, S., et al., "TNF-α and TNF-α Receptor 1 Upregulation in GLIA and Neurons After Nerve Injury. Studies in Murine DRG and Spinal Cord," 13, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C93 | Ohtori, S., et al., "TNF-α-Deficient Mice Have Fewer Macrophages in Injured Nerve and Reduced Glial Activation in DRG and Spinal Cord," 250, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C94 | Okuma, M., et al., "Rotary Cell Culture System Stimulates Annulus Fibrosus Cell Proliferation but Suppresses Proteoglycan Metabolism," 164, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| # ¹⁷ | C95 | Pacifici, R., "Editorial: Cytokines, Estrogen, and Postmenopausal Osteoporosis-The Second Decade," Endocrinology, 139(6):2659-2661 (1998). |
| | C96 | Pederson, A.W., et al., "Thermal Assembly of a Biomimetic Mineral/Collagen Composite," Biomaterials, 24:4881-4890 (2003). |
| | C97 | Richardson, S., et al., "Human Bone Marrow Mesenchymal Stromal Cells as a Source of Chondrocytes for Treatment of Intervertebral Disc Degeneration," 27, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C98 | Risbud, M. V., et al., "Mesenchymal Stem Cells Respond to Their Microenvironment In Vitro to Assume Nucleus Pulposus-Like Phenotype," 26, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| | C99 | Rodan, G.A., et al., "Therapeutic Approaches to Bone Diseases," Science, 289:1508-1514 (2000). |

| | |
|----------|---------------------|
| EXAMINER | DATE CONSIDERED |
| | |
| | |

| PTO-1449 REPRODUCED | ATTORNEY DOCKET NO. 3518.1015-000 | APPLICATION NO. 10/630,227 | | |
|-----------------------------------------------------------------|----------------------------------------|----------------------------|---------------------------|--|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION | FIRST NAMED INVENTOR Thomas M. DiMauro | FILING DATE July 30, 20 | FILING DATE July 30, 2003 | |
| March 9, 2006 (Use several sheets if necessary) | EXAMINER S.H. Shafer | CONFIRMATION NO. 8291 | GROUP 1647 | |

| | OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) |
|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| C100 | Sakai, D., et al., "Autologous Transplantation of Mesenchymal Stem Cells for Disc Repair," 24, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C101 | Sakai, D., et al., "Transplantation of Mesenchymal Stem Cells Embedded in Atelocollagen® Gel to the Intervertebral Disc: A Potential Therapeutic Model for Disc Degeneration," Biomaterials, 24: 3531-3541 (2003). |
| C102 | Schatteman, L., et al., "Treatment of Refractory Inflammatory Monoarthritis in Ankylosing Spondylitis by Intraarticular Injection of Infliximab," <i>The Journal of Rheumatology</i> , 33:1 82-85 (2006). |
| C103 | Sobajima, S., et al., "Stem Cell Therapy for Degenerative Disc Disease: An In-Vitro Feasibility Study," 43, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C104 | Stern, S., et al., "Human Intervertebral Disc Cell Culture for Disc Disorders," Clin. Orthop., 419:238-244 (2004). |
| C105 | Takada, T., et al., "IL-6 Production was Upregulated by Interaction Between Disc Tissue and Macrophages," 41, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C106 | Takegami, K., et al., "Osteogenic Protein-1 Enhances Matrix Replenishment by Intervertebral Disc Cells Previously Exposed to Interleukin-1," Spine, 27(12):1318-1325 (2002). |
| C107 | Tobinick, E.L. "Targeted Etanercept for Discogenic Neck Pain: Uncontrolled, Open-Label Results in Two Adults," Clin. Thera., 25(4):1211-1218 (2003). |
| C108 | Tsuji, T., et al., "Age-Related Changes in M-RNA Expression of Various Regulatory Factors in Rabbit Intervertebral Disc," 81, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| C109 | Vahle, J.L., et al., "Skeletal Changes in Rats Given Daily Subcutaneous Injections of Recombinant Human Parathyroid Hormone (1-34) for 2 Years and Relevance to Human Safety," Toxicol. Pathol., 30(3):312-321 (2002). |
| C110 | Weiler, C., et al., "Expression of TNF-α in Autopsy and Biopsy Specimens of Intervertebral Discs of Various Age and Degeneration," 233, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |
| CIII | Xie, X., et al., "Treatment of Spondylodiscitis Intravenous Versus Percutaneous Intradiscal Applications of Antibiotics: An Experimental Study in Rabbits," 120, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). |

| EXAMINER | DATE CONSIDERED | |
|----------|-----------------|--|
| | • | |
| | | |

| PTO-1449 REPRODUCED | 1 | | PLICATION NO. /630,227 | |
|-------------------------------------------------------------------------------------------------------------------|----------------------------------------|---------------|---------------------------|---------------|
| SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION March 9, 2006 (Use several sheets if necessary) | FIRST NAMED INVENTOR Thomas M. DiMauro | | FILING DATE July 30, 2003 | |
| | EXAMINER S.H. Shafer | CONFI 8291 | RMATION NO. | GROUP 1647 |

| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) | | |
|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| C112 | Yabuki, S., et al., "Prevention of Compartment Syndrome in Dorsal Root Ganglia Caused by Exposure to Nucleus Pulposus," Spine, 26(8):870-875 (2001). | |
| C113 | Yaffe, A., et al., "Combined Local Application of Tetracycline and Bisphosphonate Reduces Alveolar Bone Resporption in Rats," J. Periodontol, 74:1038-1042 (2003). | |
| C114 | Yoon, S. T., et al., "LMP-1 Upregulates Proteoglycan Synthesis in Intervertebral Disc Cells Through a BMP Mediated Process," 31, Abstracts of the 30th Annual Meeting of the International Society for the Study of the Lumbar Spine, Vancouver, Canada (May 2003). | |
| C115 | http://arthritis.com/od/kneetreatments/g/viscosupplement_p.htm, 12-09-2005. | |